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EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/085,117	MORRIS ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-27,29 and 32-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,29 and 32-36* is/are rejected.

7)☒ Claim(s) *29 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 2/23/07 in response to the Office Action of 8/28/06 are acknowledged and have been entered.

Claims 32-36 have been added by Applicant.

Claims 24-27, 29, and 32-36 are pending.

Claims 24-27 and 29 have been amended by Applicant.

Claims 24-27, 29, and 32-36 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections necessitated by amendments.

Objections Withdrawn

The Objections set-forth in the Office Action of 8/28/06 have been withdrawn.

Rejections Withdrawn

The rejection of claims 24-27 and 29 under 35 U.S.C. 112, second paragraph, for recitation of "...an unaffected individual..." is withdrawn.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, for reciting "the level of mRNA in (a)" is withdrawn.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, for reciting "a level of the mRNA in a second sample" is withdrawn.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, for reciting "a level of the mRNA in a third sample" is withdrawn.

The rejection of claims 24-27 and 29 under 35 U.S.C. 102(b) is withdrawn.

Response to Arguments

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-26 remain rejected under 35 U.S.C., second paragraph, for the reasons stated in the Office Action of 8/28/06 and for the reasons set-forth below.

The Office Action of 8/28/06 contains the following text:

"Claim 24 and dependant claims 25-26 are rejected because claim 24 recites: "...a decrease of at least 50% between the level of mRNA in (a) and the level of mRNA in the second or the third sample ...". It is unclear from which sample a decrease in expression would be indicative of cancer or a predisposition to cancer. Further, it is unclear from which sample a measurement is calculated in order to determine how much expression constitutes a 50% decrease. Given the above reasons, the metes and bounds of the claims cannot be determined. "

In response to the Office Actin of 8/28/06, claim 24 has been amended to recite "...a decrease of at least 50% between the level of the nucleotide sequence in (a) and

the level of the nucleotide sequence in the second sample indicates the patient has colon cancer". The Reply of 2/23/07 further states that the claims specify there is a 50% decrease in the patient sample as compared to the second sample.

The amendments to the claims and the statements found in the Reply of 2/23/07 have been carefully considered, but are not deemed persuasive. It remains unclear which sample would exhibit a decrease of at least 50%, as compared to the other sample, in the claimed method of determining the presence of colon cancer. Essentially, it is unclear whether colon cancer tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to normal colon tissue *or* whether normal colon tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to colon cancer tissue.

35 USC § 112, second paragraph

Claims 27 and 29 remain rejected under 35 U.S.C., second paragraph, for the reasons stated in the Office Action of 8/28/06 and for the reasons set-forth below.

The Office Action of 8/28/06 contains the following text:

"Claim 27 and dependant claims 28-31 are rejected because claim 27 recites: "...a decrease of at least about 50% between the level of CA gene expression in (a) and the level of CA gene expression in the second or the third sample ...". It is unclear from which sample a decrease in expression would be indicative of cancer or a predisposition to cancer. Further, it is unclear from which sample a measurement is

calculated in order to determine how much expression constitutes a 50% decrease. Given the above reasons, the metes and bounds of the claims cannot be determined."

In response to the Office Actin of 8/28/06, claim 27 has been amended to recite "...a decrease of at least 50% between the level of the nucleotide sequence in (a) and the level of the nucleotide sequence in the second sample indicates the patient has colon cancer". The Reply of 2/23/07 further states that the claims specify there is a 50% decrease in the patient sample as compared to the second sample.

The amendments to the claims and the statements found in the Reply of 2/23/07 have been carefully considered, but are not deemed persuasive. It remains unclear which sample would exhibit a decrease of at least 50%, as compared to the other sample, in the claimed method of determining the presence of colon cancer. Essentially, it is unclear whether colon cancer tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to normal colon tissue *or* whether normal colon tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to colon cancer tissue.

35 USC § 112, second paragraph

Claim 29 remains rejected under 35 U.S.C., second paragraph, for the reasons stated in the Office Action of 8/28/06 and for the reasons set-forth below.

The Office Action of 8/28/06 contains the following text:

"Claim 29 is rejected for reciting: "...wherein the decrease between the level of CA gene expression in (a) and the level of the CA gene expression in the second or

third sample ...". It is unclear from which sample a decrease in expression would be indicative of cancer or a predisposition to cancer. Further, it is unclear from which sample a measurement is calculated in order to determine how much expression constitutes a 100% decrease. Given the above reasons, the metes and bounds of the claims cannot be determined."

In response to the Office Actin of 8/28/06, claim 29 has been amended to recite "...wherein the decrease between the level of the nucleotide sequence in (a) and the level of the nucleotide sequence in the second sample is at least 100% ...". The Reply of 2/23/07 further states that the claims specify there is a 100% decrease in the patient sample as compared to the second sample.

The amendments to the claims and the statements found in the Reply of 2/23/07 have been carefully considered, but are not deemed persuasive. It remains unclear which sample would exhibit a decrease of at least 100%, as compared to the other sample, in the claimed method of determining the presence of colon cancer. Essentially, it is unclear whether colon cancer tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to normal colon tissue *or* whether normal colon tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to colon cancer tissue.

35 USC § 112, first paragraph (Enablement Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-27 and 29 remain rejected and newly-added claims 32-36 are rejected under 35 U.S.C. 112 first paragraph, for failing to comply with the enablement requirement, for the reasons stated in the Office Action of 8/28/06 and for the reasons set-forth below.

The Office Action of 8/28/06 contains the following text:

"..., while being enabling for diagnosing prostate cancer comprising detecting an increase in Egr-1 gene expression (SEQ ID NO:167) in a prostate tissue sample as compared to Egr-1 gene expression (SEQ ID NO:167) in a normal prostate tissue, does not reasonably provide enablement for a method of diagnosing every other type of cancer comprising detecting just any type of change in expression of just any CA gene in just any type of sample, as compared to any type of control. Further, the specification does not enable *any* kind of diagnostic assay wherein one would be able to predictably determine whether someone has a predisposition to any cancer by measuring expression of Egr-1 (SEQ ID NO:167) in any sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the

breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are broadly drawn to a method of diagnosing every type of cancer and methods of determining whether a person has a predisposition for every type of cancer comprising detecting just any type of change in just any CA gene in just any type of sample, as compared to any type of control.

The specification discloses that SEQ ID NO:167 is a cancer associated (CA) nucleic acid (page 10 lines 9-12 and table 29, in particular). The specification further discloses that CA nucleic acids are nucleic acids that were identified through use of oncogenic retroviruses, whose sequences insert into the genome of lymphatic tissue resulting in carcinoma (page 3 lines 17-29 and page 7 lines 20-24, in particular). Further, the specification prophetically states that "oncogenes that are identified in one type of cancer such as lymphoma or leukemia have a strong likelihood of being involved in other types of cancers as well..." (page 3 lines 21-24).

The specification lacks any working example showing that SEQ ID NO:167 is aberrantly expressed in any cancer type. Further, undue experimentation would be required to determine whether the expression level of SEQ ID NO:167 is indicative of every carcinoma or indicative of a predisposition for every cancer. However, the teachings of Eid et al (Cancer Research, 6/1/98, 58:2461-2468) demonstrate that an increase in Egr-1 expression in prostate biopsies from a subject, as compared to Egr-1 expression in normal prostate tissue, is indicative that said subject has prostate cancer (Figure 2, in particular). The prior art does not teach or suggest that methods of

measuring Egr-1 (SEQ ID NO:167) expression could be used to determine whether a patient has a predisposition to any kind of tumor with any predictability of success.

The state of the prior art dictates that if a molecule such as a specific polynucleotide, such as that set forth in SEQ ID NO:167, is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714,

see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the polynucleotide's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the polynucleotides in any diagnostic setting without undue experimentation.

The level of unpredictability for the detection of any disease and the detection of a predisposition to any disease is quite high. Since neither the specification nor the prior art provide evidence of a universal association between the claimed method and every cancer and every type of sample, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method of diagnosing and determining whether a person has just any type of cancer or has a predisposition for just any type of cancer comprising detecting just any type of change expression in just any CA gene in just any type of sample, as compared to any type of control, and Applicant has not enabled said methods because it has not been shown that detecting every type of differential expression of every type of CA gene, as compared to every type of control, in every type of sample, could predictably be used as a universal

method to determine whether a person has just any type of cancer or is predisposed to having any type of cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed."

In response to the Office Action of 8/28/06, Applicant amended claims 24-27 and 29. Amended claims 24-27 and 29 are no longer drawn to "prognostic" methods; rather, amended claims 24-27 and 29 are drawn to methods of diagnosing colon cancer and newly-added claims 32-36 are drawn to methods of diagnosing prostate cancer. Applicant argues that no undue experimentation would be required for a person of skill in the art to practice the presently claimed methods. Applicant states that the skill in the art is quite high and that those of skill in the art would have been quite capable of measuring levels of sequences comprising SEQ ID NO:167 without undue experimentation. Applicant further states that the amended claims recite a specified degree of reduction of expression as indicative of either colon or prostate cancer. Applicant further states that the amended claims specify controls comprising non-cancerous colon or non-cancerous prostate tissue. Applicant further states that the Eid reference (Cancer Research, 6/1/98, 58:2461-2468) supports the enablement of the pending claims. Applicant indicates the Eid reference teaches one how to measure levels of Egr-1 polynucleotide and correlate levels to prostate cancer. Applicant further states that Eid discloses that in certain carcinomas (lung, breast, glioblastoma, and

ostoegenic carcinoma) absence of expression of Egr-1 is correlated with cancer. Applicant further states: "...Eid states that "Our studies demonstrated a significant increase in expression of EGR-1 in tumors with more aggressive morphology compared with less aggressive tumors." Accordingly, the difference in expression as an indicator of prostate cancer seen in Eid as compared to the present application (Eid indicates increased expression is indicative of prostate cancer while a decrease in expression is claimed in the present invention) may be a function of the nature of the tumor cells tested (i.e. aggressive tumors vs. less aggressive tumors)". Applicant further argues that the Office appears to be requiring as proof of enablement information and data outside the scope of the enablement requirement, such as data that would be required by the FDA for approval purposes.

The amendments to the claims and the statements found in the Reply of 2/23/07 have been carefully considered, but are not deemed persuasive. While being enabling for a method of diagnosing prostate cancer comprising determining the level of a nucleotide sequence comprising SEQ ID NO:167 in a patient sample comprising prostate tissue and comparing said level to the level of nucleotide sequence comprising SEQ ID NO:167 in non-cancerous prostate tissue, wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the non-cancerous prostate tissue as compared to the patient sample indicates that the patient has prostate cancer, the specification does not provide enablement for: (1) a method of diagnosing colon cancer comprising determining the level of a nucleotide sequence comprising SEQ ID NO:167 in a patient sample comprising colon tissue and comparing said level to the level of

nucleotide sequence comprising SEQ ID NO:167 in non-cancerous colon tissue, wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the non-cancerous colon tissue as compared to the patient sample indicates that the patient has colon cancer *and* wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the patient sample as compared to non-cancerous colon tissue indicates that the patient has colon cancer (see claims 24 and 27); (2) a method of diagnosing prostate cancer comprising determining the level of a nucleotide sequence comprising SEQ ID NO:167 in a patient sample comprising prostate tissue and comparing said level to the level of nucleotide sequence comprising SEQ ID NO:167 in non-cancerous colon tissue, wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the non-cancerous colon tissue as compared to the patient sample indicates that the patient has prostate cancer *and* wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the patient sample as compared to non-cancerous colon tissue indicates that the patient has prostate cancer (see claim 32); or (3) a method of diagnosing prostate cancer comprising determining the level of a nucleotide sequence comprising SEQ ID NO:167 in a patient sample comprising prostate tissue and comparing said level to the level of nucleotide sequence comprising SEQ ID NO:167 in non-cancerous prostate tissue, wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the non-cancerous prostate tissue as compared to the patient sample indicates that the patient has prostate cancer *and* wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in

the patient sample as compared to non-cancerous prostate tissue indicates that the patient has prostate cancer.

In regards to the argument that no undue experimentation would be required for a person of skill in the art to practice the presently claimed methods, the Examiner maintains that undue experimentation would be required for a person of skill in the art to practice the presently claimed methods with an expectation of success. As stated in the Office Action of 8/28/06, the level of unpredictability for the detection of any disease is quite high and the state of the art dictates that if a molecule such as a specific polynucleotide, such as that set forth in SEQ ID NO:167, is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. The disclosure does not provide a working example demonstrating that expression of a polynucleotide of SEQ ID NO:167 is indicative of colon cancer or that a comparison between the levels of expression of polynucleotides comprising SEQ ID NO:167 in a prostate sample from a patient and a non-cancerous *colon* tissue sample would predictably determine whether said patient has prostate cancer. In such an unpredictable art, the prophetic guidance disclosed in the specification does not convincingly demonstrate that the claimed method would function as predicted. Further, without demonstrating that non-cancerous prostate cancer tissue and non-cancerous colon tissue have similar levels of polynucleotides comprising SEQ ID NO:167, one of skill in the art would recognize the unpredictability of diagnosing prostate cancer by comparing the level of polynucleotides comprising SEQ

ID NO:167 in a prostate sample from a patient with level of said polynucleotides in a non-cancerous *colon* tissue. It is further noted that the quantitative method by which Eid measured levels of polynucleotides comprising SEQ ID NO:167 in prostate tumor tissue did not compare said levels of polynucleotides comprising SEQ ID NO:167 in non-cancerous colon tissue (see Table 1). It is further noted that the Northern blot taught by Eid et al was not sensitive enough to detect polynucleotides comprising SEQ ID NO:167 in prostate or colon (see Figure 1). Therefore, it is unpredictable how levels of polynucleotides comprising SEQ ID NO:167 in prostate compare to levels of said polynucleotides in colon.

In regards to the argument that the amended claims recite a specified degree of reduction of expression as indicative of either colon or prostate cancer, the amended claims do *not* recite whether decreased expression in the patient tissue sample as compared to the control sample is indicative of a cancer or whether decreased expression in the control sample as compared to the patient sample is indicative of a cancer.

In regards to the argument that Eid et al teaches that in certain carcinomas (lung, breast, glioblastoma, and ostoegenic carcinoma) absence of expression of Egr-1 is correlated with cancer, the instant claims are not drawn to lung, breast, glioblastoma, or ostoegenic carcinoma. One of skill in the art would recognize that markers for one cancer are not predictable for every other cancer. Further, the passage in Eid et al which Applicant appears to be referring discusses studies which examined growth of tissue culture lines transfected with Egr-1 and one of skill in the art would recognize that

phenotypes observed after transfecting cell lines with a certain polynucleotide do not predictably indicate whether said polynucleotide is a marker for a particular cancer. Tockman et al teaches how a diagnostic biomarker is recognized (see above).

In regards to the argument that the difference in expression as an indicator of prostate cancer seen in Eid as compared to the present application (Eid indicates increased expression is indicative of prostate cancer while Applicant argues a decrease in expression is claimed in the present invention) may be a function of the nature of the tumor cells tested (i.e. aggressive tumors vs. less aggressive tumors), the present claims are *broadly* drawn to methods wherein a decrease level of nucleotide sequence comprising SEQ ID NO:167 in a non-cancerous tissue as compared to the level of level of nucleotide sequence comprising SEQ ID NO:167 in a patient sample indicates that the patient has cancer *and* wherein a decreased level of nucleotide sequences comprising SEQ ID NO:167 in the patient sample as compared to non-cancerous tissue indicates that the patient has cancer. Further, it is noted that the disclosure does not provide a single working example and Eid et al *clearly* teaches an example that demonstrates elevated levels of nucleotide sequences comprising SEQ ID NO:167 are found in prostate tissue samples from patients with prostate cancer, as compared to levels of said sequences in non-cancerous prostate tissue samples. The art does not hint or suggest that a decrease in expression of nucleotide sequence comprising SEQ ID NO:167 in prostate tissue samples, as compared to any type of control, would predictably indicate that the patient has prostate cancer. In fact, the teachings of Eid et al *strongly* argue otherwise.

In regards to the argument that the Office appears to be requiring as proof of enablement information and data outside the scope of the enablement requirement, such as data that would be required by the FDA for approval purposes, Examiner agrees that the requirements for FDA approval are different than the requirements of 35 U.S.C. 112, first paragraph. However, 35 U.S.C. 112, first paragraph, does have requirements. For instance, the specification must enable one to perform the claimed invention without undue experimentation. As stated above, factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. This factors are addressed above.

New Objections Necessitated by Amendments

Claims 29 and 36 are objected to for failing to further limit the subject matter of the claims on which they depend. Rather than providing any type of limitation to the claimed methods, claims 29 and 36 appear to recite *results* obtained by the claimed methods. Proper correction is required.

New Rejections Necessitated by Amendments

35 USC § 112, first paragraph (Written Description Rejection)

Claims 24, 25, 27, 29, 32, 33, 35, and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of: (1) a genus of nucleotide sequences comprising a sequence at least 98% identical to SEQ ID NO:167 and complements thereof; (2) a genus of nucleotide sequences comprising a sequence at least 99% identical to SEQ ID NO:167; and (3) a genus of complements of nucleotide sequences comprising SEQ ID NO:167. However, the written description in this case only sets forth nucleotide sequences comprising SEQ ID NO:167 and the *full* complement thereof. The specification does not disclose any other variant of SEQ ID NO:167 or fragments of complements of SEQ ID NO:167 or variants thereof as broadly encompassed in the claims.

The prior art of Monia et al (US Patent 6,008,048; 12/28/99) teaches a sequences 100% identical to instant SEQ ID NO:1; however, Monia et al does not teach a representative number of species encompassed by the genera of the claimed method.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43

USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genera. That is, the specification provides neither a representative number of sequences that encompass the genera nor does it provide a description of structural features that are common to the genera. Further, in regards to genera encompassing variants and fragments, Applicant is directed to Example 13 of the Synopsis of Application of Written Description Guidelines (http://www.uspto.gov/web/menu/written.pdf), which addresses claims drawn to a genus of polypeptide variants. Example 13 states that even when a specification discloses that changes which produce variants are routinely done in the art, the specification and the claims do not provide any guidance as to precisely what changes should be made. Structural features that could distinguish the compounds of the claimed genera from others not encompassed by the genera are missing from the disclosure. No common structural attributes identify the members of the genera. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not

general, guidance is needed. Since the disclosure fails to describe common attributes or characteristics that identify members of the genera, and because the genera are highly variant, the disclosure of SEQ ID NO:167 is insufficient to describe the genera. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genera as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genera, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification

provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

New Matter

Claims 25 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claims 25 and 33 recite methods wherein a sequence is at least 99% identical to SEQ ID NO:167. Descriptions of sequence that are at least "99%" identical to SEQ ID NO:167 are not found in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 35-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Eid et al (Cancer Research 58, 2461-2468) as evidenced by Monia et al (US Patent 6,008,048; 12/28/99).

Eid et al teaches a method of diagnosing prostate cancer in a patient comprising determining the level of Egr-1 nucleotide sequence in a prostate tissue test sample and comparing said level to a level of the nucleotide sequence in a non-cancerous prostate tissue sample, wherein a decrease of at least 50% between the level of the nucleotide sequence in the test sample and the level of the nucleotide sequence in the non-cancerous sample indicates that the patient has prostate cancer (Table 1, in particular). Note that the claims do not recite which sample exhibits the decrease. However, note that Eid et al teaches that a decreased the level of Egr-1 nucleotide sequence in the non-cancerous prostate tissue as compared to the patient sample indicates that the patient has prostate cancer. As evidenced by Monia et al, Egr-1 consists of the polynucleotide sequence set-forth in instant SEQ ID NO:167 (see attached sequence comparison of SEQ ID NO:47 taught by Monia et al and instant SEQ ID NO:167, in particular). Further, when the level of polynucleotides comprising the polynucleotide sequence set-forth in instant SEQ ID NO:167 in normal prostate tissue is set at 100%, Eid et al further teaches that the level of said polynucleotides in normal prostate tissue is decreased greater than 100%, as compared to levels of said polynucleotides in prostate cancer tissues (see Table 1, in particular).

Summary

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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